

REMARKS

Applicants believe that this application has been amended in a manner that places it in condition for allowance at the time of the next Official Action.

Claims 36 and 39-53 are pending in the present application. Claims 36 and 39-52 have been amended to more particularly point out and distinctly claim the present invention. New claim 53 has been added. Support for new claim 53 may be found in original claim 36 and in the present specification at page 9, line 32 to page 10, line 11.

In the outstanding Official Action, claims 37 and 38 were objected to under 37 CFR 1.72(c) as allegedly being of improper dependent form. In the interest of advancing prosecution, claims 37 and 38 have been canceled. Thus, it is believed that this objection has been obviated.

Claims 36-46 were rejected under 35 USC 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the present invention.

In imposing the rejection, the Official Action alleged that the term "a DNA sequence comprising a gene expressing a fluorescent protein fused with a gene for the target protein" was indefinite. However, applicants believe that this term is definite to one of ordinary skill of art. Moreover, the

Examiner's attention is directed to page 3, line 9, wherein the description as to how the claimed invention is constructed begins in detail.

The outstanding Official Action rejected claims 38 and 50 for not providing the full definitions for the abbreviations "EYFP", "EGFP", and "ECFP". Claim 38 has been canceled. The full definitions for the abbreviations recited in claim 50 has been provided. Thus, it is believed that these rejections have been obviated.

The Official Action also rejected claim 37 for being indefinite. However, as noted above, claim 37 has been canceled. Thus, it is believed that the rejection concerning claim 37 has been rendered moot.

Claims 36-48 were rejected for allegedly being incomplete for omitting essential steps. This rejection is respectfully traversed.

Claims 36-48 have been amended to recite a further step of measuring the fluorescent energy transfer when quantifying the non-covalent interactions. Thus, it is believed that claims 36-48 are definite to one of ordinary skill in the art.

In the outstanding Official Action, claims 10-21, 27, 28 and 32-35 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly not complying with the written

description requirement. This rejection is respectfully traversed.

Applicants believe that the Official Action fails to meets its burden in showing that that the claimed invention is not supported by a sufficient written description. In imposing the rejection, the Official Action alleges that the specification does not disclose the necessary starting materials. However, the Official Action fails to identify what starting materials are not provided by the present disclosure or articles cited therein. Indeed, the Official Action does not provide any rationale or basis as to why the claimed invention is not supported by the present disclosure other than each and every possible starting material might not be disclosed.

In this regard, the Examiner is reminded that it is not necessary that every last detail of an invention be described, by working example or otherwise. *Ex parte Wolters et al.*, 214 USPQ 735 (POBA 1979). Indeed, the specifications is not intended to be a production specification or batch record.

As to the declaration submitted by Jean-Luc Galzi, applicants note that the Examiner must consider extrinsic factual evidence relevant to the issue of adequacy of the "written description". Moreover, an applicant can present a declaration of an expert which states how one skilled in the art would interpret an example of the claimed invention to establish that

the requisite description of the invention is present. *In re Alton*, 76 F. 3d 1168, 37 USPQ 2d 1578 (CAFC 1996). Applicants believe that the declaration by Jean-Luc Galzi clearly shows that one of ordinary skill in the art would find that the applicant was in possession of the claimed invention at the time the application was filed. While the Official action dismisses the declaration because the declarant is an inventor, the Official Action does not present any evidence that contradicts the statements of the declarant. Rather, the Official Action relies on the unsupported allegation that the specification does not show that applicants were in possession of the claimed invention at the time the application was filed.

Thus, it is believed that the Official Action fails meet its burden in showing that the claimed invention is not supported by a sufficient written description.

Claims 36-52 were rejected under 35 USC 112, first paragraph, as allegedly failing to comply with the enablement requirement. This rejection is respectfully traversed.

In imposing the rejection, the outstanding Official Action contends that a review of the disclosure finds 11 examples. Of those 11 examples, the Official Action contends that the appropriate reaction conditions and starting materials are not provided. However, the Examiner is reminded that a patent application need not teach, and preferably omits, what is

well known in the art, *Spectra-physics, Inc. vs. Coherent, Inc.*, 827 F.2d 1524, 3 USPQ 2d 1737 (CAFC 1987). Moreover, applicants believe that the Official Action does not provide any evidence to support the contention.

Applicants remind the Examiner that a specification purporting to contain an enabling description of a claimed invention is presumed enabling, unless there is reason to doubt the objective truth thereof. Indeed, the PTO has the burden of giving reasons, supported by the record as a whole, why the specification as a whole is not enabling, e.g., entails undue experimentation. *In re Wright*, 999 F.2d 1557, 27 USPQ 2d 1510 (CAFC 1993). Thus, as the Official Action fails to provide any evidence as to why the present specification is not enabling, applicants believe the outstanding Official Action fails to meet its burden in showing that the present specification is not an enabling description.

More importantly, applicants believe that the present disclosure is enabling for the claimed invention. Applicants believe that one of the more relevant examples in the present specification is Example 5. Example 5 relates to the detection and quantification of non-covalent interactions between the target protein and one of its ligands. Applicants believe that the starting materials and reactions are provided in Example 5.

Indeed, some of the technical elements which the outstanding Official Action contends are not provided by the present specification are provided as follows:

- a) Example 1 (as well as Example 2) fully describes the mode of preparation of a fluorescent receptor by means of fusing its gene with that of GFP;
- b) Example 3 details the protocol for expressing the fluorescent receptor in mammalian cells and all procedures to detect expression (fluorescence measurements, radioligand binding) and function (cytosolic calcium determination) of the fluorescent receptor;
- c) Example 4 gives all technical information about the preparation of a fluorescent ligand for the receptor including experimental protocols to label the ligand with several fluorophores (bodipy, coumarin, eosin or sulforhodamine) and to purify the fluorescent ligand; and
- d) Example 5 extensively describes the approaches to detect the interaction between the fluorescent ligand and the fluorescent receptor including i) standard radioligand binding assay as a control, and ii) fluorescence resonance energy transfer detection at equilibrium or in real time. Example 5, in addition, describes how binding can be quantified (saturation experiment) and how non-labeled molecules can compete with the

fluorescent ligand for binding to the receptor, in a quantitative manner.

The subsequent examples are variants of Examples 1-5 which show that other expression systems can be used (Example 6 compared to 3), that other proteins (Examples 7-9 compared to 1 and 2) as well as other ligands (Example 10 compared to 4) can be fluorescently labeled, and finally that other detection systems, using fluorescently labeled proteins, can be considered (Example 11).

Example 5 also explains how new molecules binding to a receptor can be discovered. These new molecules, which are not fluorescently labeled, will compete with the fluorescent ligand if they exhibit affinity for the receptor. If such a molecule is present in the assay, then the intensity of energy transfer between the fluorescent receptor and the fluorescent ligand will be lower, as a result of competition. The intensity of energy transfer decrease will in addition provide information on the affinity of the new molecule, since at a given concentration it will occupy a proportion of receptor sites that is directly dependent on its affinity.

Thus, it is believed that the claimed invention is enabled by the present disclosure.

In view of the present amendment and the foregoing remarks, therefore, it is believed that this application is now

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in condition for allowance, with claims 36 and 39-53, as presented. Allowance and passage to issue on that basis are accordingly respectfully requested.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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